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WHAT IS CLAIMED IS:

1. A method for predicting irritant potential of a candidate substance comprising:
a) providing a mammalian cell that releases a nucleotide in response to an
10 inflammatory agent;
b) culturing said cell with a candidate substance; and
c) determining nucleotide release from said cell,
wherein an increase in nucleotide release from said cell, as compared to nucleotide
release in the absence of said candidate substance, indicates that said candidate substance
15 is an irritant.
2. The method of claim 1, wherein said cell is a fibroblast.
3. The method of claim 1, wherein said cell is a keratinocyte.
- 20 4. The method of claim 3, wherein said cell is a human keratinocyte.
5. The method of claim 3, wherein said cell is a mouse keratinocyte.
- 25 6. The method of claim 5, wherein said cell is a PAM 212 cell.
7. The method of claim 1, wherein said nucleotide is ATP and/or ADP and/or AMP,
UTP and/or UDP and/or UMP, CTP and/or CDP and/or CMP, TTP and/or TDP and/or
TMP, or GTP and/or GDP and/or GMP.
- 30 8. The method of claim 1, wherein said nucleotide is ATP and/or ADP and/or AMP.
9. The method of claim 1, wherein said nucleotide is UTP and/or UDP and/or UMP.

- 5 10. The method of claim 1, wherein determining nucleotide release from said cell comprises measuring nucleotide concentration in the cell culture medium.
11. The method of claim 10, wherein measuring nucleotide concentration comprises an enzymatic assay.
- 10 12. The method of claim 11, wherein said enzymatic assay is a luciferin-luciferase assay.
13. The method of claim 10, wherein measuring nucleotide concentration comprises
- 15 thin layer chromatography.
14. The method of claim 1, wherein said candidate substance is a naturally-occurring compound.
- 20 15. The method of claim 1, wherein said candidate substance is a man-made compound.
16. The method of claim 1, further comprising measuring nucleotide release from said cell in the absence of said candidate substance.
- 25 17. The method of claim 1, further comprising a control comprising:
 - a) contacting said cell with a known irritant; and
 - b) measuring nucleotide release from said cell.
- 30 18. A method for preventing an inflammatory response in a subject comprising administering to said subject a composition comprising a NTPDase.
19. The method of claim 18, wherein said NTPDase is an ATPase and/or ADPase, an UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase
- 35 and/or GDPase.

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20. The method of claim 18, wherein said NTPDase is selected from the group consisting of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-ATPase and ecto-uridine diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan and potato apyrase.

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21. The method of claim 18, wherein said inflammatory response is chemical skin irritation, and said NTPDase is applied as a topical formulation.

22. The method of claim 18, wherein said inflammatory response is mucosal irritation, and said NTPDase is applied as an oral, intranasal, intratracheal, intraesophageal, intrabronchial, intra-vaginal or rectal formulation.

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23. The method of claim 18, wherein said inflammatory response is caused by a pro-inflammatory leukocyte.

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24. The method of claim 18, wherein said inflammatory response is caused by a soluble pro-inflammatory factor.

25. The method of claim 24, wherein said soluble pro-inflammatory factor is a cytokine, a prostaglandin, or a histamine.

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26. A method for treating an inflammatory response in a subject comprising administering to said subject a composition comprising a NTPDase.

27. A method for preventing an inflammatory response in a subject comprising administering to said subject an expression construct comprising a DNA segment encoding a NTPDase under the control of a promoter active in cells of said subject.

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28. The method of claim 27, wherein said expression construct is a viral expression construct.

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29. The method of claim 27, wherein said viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a herpesvirus, a polyoma virus, and a vaccinia virus.

10 30. The method of claim 27, wherein said expression construct is a non-viral expression construct.

31. The method of claim 30, wherein said non-viral expression construct is administered as a naked DNA.

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32. The method of claim 30, wherein said non-viral expression construct is administered in a liposomal formulation.

33. The method of claim 27, wherein said NTPDase is an ATPase and/or ADPase, an
20 UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase and/or GDPase.

34. The method of claim 27, wherein said NTPDase is selected from the group
consisting of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-
25 ATPase and ecto-uridine diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan and potato apyrase.

35. The method of claim 27, wherein said inflammatory response is chemical skin irritation, and said NTPDase is applied as a topical formulation.

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36. The method of claim 27, wherein said inflammatory response is mucosal irritation, and said NTPDase is applied as an oral, intranasal, intratracheal, intraesophageal, intrabronchial, intra-vaginal or rectal formulation.

- 5 37. The method of claim 27, wherein said inflammatory response is caused by a pro-inflammatory leukocyte.
38. The method of claim 27, wherein said inflammatory response is caused by a soluble pro-inflammatory factor.
- 10 39. The method of claim 38, wherein said soluble pro-inflammatory factor is a cytokine, a prostaglandin, or a histamine.
40. A method for treating an inflammatory response in a subject comprising
15 administering to said subject an expression construct comprising a DNA segment encoding a NTPDase under the control of a promoter active in cells of said subject.
41. A method of screening for modulators of inflammation comprising:
 - a) providing a cell that expresses a NTPDase;
 - 20 b) contacting said cell with a candidate substance; and
 - c) determining the effect of said candidate substance on said NTPDase expression in said cell,wherein a change in the expression of a NTPDase in said cell, as compared to NTPDase expression in the absence of said candidate substance, indicates that said candidate
25 substance is a modulator of a NTPDase expression, and therefore a modulator of inflammation.
42. The method of claim 41, wherein said cell is a dendritic cell.
- 30 43. The method of claim 42, wherein said dendritic cell is a Langerhans cell or cell line.
44. The method of claim 41, wherein said cell comprises an expression construct comprising a DNA segment encoding said NTPDase under the control of a promoter
35 active in said cell.

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45. The method of claim 41, wherein determining comprises measuring NTPDase levels in said cell.

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46. The method of claim 41, wherein measuring comprises measuring a NTPDase on the surface of said cell.

47. The method of claim 46, comprising an enzyme linked immunoassay using an enzyme-labeled anti-NTPDase antibody.

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48. The method of claim 47, wherein the anti-NTPDase antibody is an anti-ATPase and/or anti-ADPase antibody, an anti-UTPase and/or anti-UDPase antibody, a anti-CTPase and/or anti-CDPase antibody, a anti-TTPase and/or anti-TDPase antibody, or a anti-GTPase and/or anti-GDPase antibody.

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49. The method of claim 47, comprising fluorescent activated cell sorting of cells using a fluorescent-labeled anti-NTPDase antibody.

50. The method of claim 41, wherein determining comprises measuring a NTPDase mRNA level in said cell.

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51. The method of claim 50, wherein measuring comprises Northern blotting.

52. The method of claim 50, wherein measuring comprises quantitative RT-PCR.

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53. The method of claim 41, wherein determining comprises measuring NTPDase activity of said cell.

54. The method of claim 41, wherein said modulator is an inhibitor of inflammation.

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55. The method of claim 41, wherein said modulator is a promoter of inflammation.

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56. A method of screening for modulators of inflammation comprising:

- a) providing a cell that comprises an expression construct comprising a DNA segment encoding a screenable marker under the control of a promoter for a NTPDase;
- 10 b) contacting said cell with a candidate substance; and
- c) determining the effect of said candidate substance on expression of said selectable marker,

wherein a change in the expression of said selectable marker, as compared to selectable marker expression in the absence of said candidate substance, indicates that said
 15 candidate substance is a modulator of NTPDase promoter expression, and therefore a modulator of inflammation.

57. The method of claim 56, wherein said NTPDase is selected from the group consisting of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-
 20 ATPase and ecto-uridine diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan and potato apyrase.

58. The method of claim 56, wherein said screenable marker is an enzyme and determining comprises measuring enzyme activity.

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59. The method of claim 56, wherein said modulator is an inhibitor of inflammation.

60. The method of claim 56, wherein said modulator is a promoter of inflammation.

30 61. A method of screening for a modulator of inflammation comprising:

- a) providing a cell that expresses a membrane bound NTPDase, or ecto-NTPDase in a culture solution comprising a nucleotide;
- b) contacting said cell with a candidate substance; and
- 35 c) determining the effect of said candidate substance on nucleotide levels in said culture solution,

5 wherein a change in the nucleotide levels in said culture solution, as compared to nucleotide levels in the absence of said candidate substance, indicates that said candidate substance is a modulator of NTPDase activity, and therefore a modulator of inflammation.

10 62. The method of claim 61, wherein said NTPDase is an ATPase and/or ADPase, an UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase and/or GDPase.

63. The method of claim 61, wherein said cell expresses an ATPase.

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64. The method of claim 61, wherein said cell expresses an ADPase.

65. The method of claim 61, wherein said cell expresses an UTPase.

20 66. The method of claim 61, wherein said cell expresses an UDPase.

67. The method of claim 61, wherein said nucleotide is ATP and/or ADP and/or AMP, UTP and/or UDP and/or UMP, CTP and/or CDP and/or CMP, TTP and/or TDP and/or TMP, or GTP and/or GDP and/or GMP.

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68. The method of claim 61, wherein said nucleotide is ATP and/or ADP and/or AMP.

69. The method of claim 61, wherein said nucleotide is UTP and/or UDP and/or
30 UMP.

70. The method of claim 61, wherein said modulator is an inhibitor of inflammation.

71. The method of claim 61, wherein said modulator is a promoter of inflammation.
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- 5 72. The method of claim 68, wherein AMP levels are detected by chromatographic methods.
73. A method for treating a hyperactive immune response in a subject comprising administering to said subject a composition comprising a NTPDase inhibitor.
- 10 74. The method of claim 73, wherein said NTPDase inhibitor is an ATPase inhibitor and/or ADPase inhibitor, an UTPase inhibitor and/or UDPase inhibitor, a CTPase inhibitor and/or CDPase inhibitor, a TTPase inhibitor and/or TDPase inhibitor, or a GTPase inhibitor and/or GDPase inhibitor.
- 15 75. The method of claim 73, wherein said NTPDase inhibitor is an NTPDase antagonist, an anti-NTPDase antibody, an antisense oligonucleotide, or a chemical substance.
- 20 76. The method of claim 73, wherein the NTPDase inhibitor is an NTPDase antagonist.
77. The method of claim 76, wherein the NTPDase antagonist is Azide, Evans Blue, Suramin, PPADS, DEPC, P-CMPS, P-HMB, NP-40, FSBA.
- 25 78. The method of claim 75, wherein the anti-NTPDase antibody is an anti-ATPase and/or anti-ADPase antibody, an anti-UTPase and/or anti-UDPase antibody, a anti-CTPase and/or anti-CDPase antibody, a anti-TTPase and/or anti-TDPase antibody, or a anti-GTPase and/or anti-GDPase antibody.
- 30 79. The method of claim 75, wherein the antisense oligonucleotide comprises a nucleic acid that is complementary to a nucleic acid sequence encoding an ATPase and/or ADPase, an UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase and/or GDPase, or a fragment thereof.

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- 5 80. The method of claim 73, wherein said NTPDase inhibitor is an inhibitor of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-ATPase and ecto-uridine diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan or potato apyrase.
- 10 81. The method of claim 73, wherein said hyperactive immune response is an allergic reaction.
82. The method of claim 81, wherein said allergic reaction is allergic contact dermatitis, atopic dermatitis, allergic rhinitis (hay fever), bronchial asthma.
- 15 83. The method of claim 73, wherein said hyperactive immune response is an autoimmune disease.
84. The method of claim 83, wherein said autoimmune disease is Addison's disease, alopecia, ankylosing spondylitis, antiphospholipid syndrome, Behcet's disease, chronic fatigue syndrome, Crohn's disease, ulcerative colitis, diabetes, fibromyalgia, Goodpasture syndrome, Graves' disease, idiopathic thrombocytopenic purpura, lupus, Meniere's multiple sclerosis, myasthenia gravis, pemphigus vulgaris, primary biliary cirrhosis, psoriasis, rheumatoid arthritis, rheumatic fever, sarcoidosis, scleroderma, vasculitis, 25 vitiligo, or Wegener's granulomatosis.
85. The method of claim 73, wherein said NTPDase inhibitor is administered by topical, oral, intranasal, intratracheal, intraesophageal, intrabronchial, intravenous, intraarterial, intramuscular, subcutaneous, intra-vaginal or rectal routes.
- 30 86. A method for preventing a hyperactive immune response in a subject comprising administering to said subject a composition comprising a NTPDase inhibitor.
87. A method for treating or preventing a hyperactive immune response in a subject 35 comprising administering to said subject an expression construct comprising a DNA

5 segment encoding a NTPDase inhibitor under the control of a promoter active in cells of said subject.

88. The method of claim 87, wherein said NTPDase inhibitor is an ATPase inhibitor and/or ADPase inhibitor, an UTPase inhibitor and/or UDPase inhibitor, a CTPase
10 inhibitor and/or CDPase inhibitor, a TTPase inhibitor and/or TDPase inhibitor, or a GTPase inhibitor and/or GDPase inhibitor.

89. The method of claim 87, wherein said NTPDase inhibitor is an inhibitor of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-ATPase and ecto-uridine
15 diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan or potato apyrase.

90. The method of claim 87, wherein the NTPDase inhibitor is an antisense molecule.

20 91. The method of claim 90, wherein the antisense oligonucleotide comprises a nucleic acid that is complementary to the nucleic acid sequence encoding an ATPase and/or ADPase, an UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase and/or GDPase or a fragment thereof.

25 92. The method of claim 87, wherein said expression construct is a viral expression construct.

93. The method of claim 87, wherein said viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a
30 herpesvirus, a polyoma virus, and a vaccinia virus.

94. The method of claim 87, wherein said expression construct is a non-viral expression construct.

5 95. The method of claim 87, wherein said non-viral expression construct is administered as a naked DNA.

96. The method of claim 95, wherein said non-viral expression construct is administered in a liposomal formulation.

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97. A method of screening for modulators of NTPDase-mediated immune responses comprising:

- a) providing a cell that expresses a membrane bound NTPDase or an ecto-NTPDase;
- 15 b) contacting said cell with a candidate substance; and
- c) determining the effect of the candidate substance on the NTPDase level in said cell,

wherein a change in the level of a NTPDase in said cell, as compared to NTPDase level in the absence of the candidate substance, indicates that the candidate substance is a
20 modulator of NTPDase level, and therefore a modulator of NTPDase-mediated immune responses.

98. The method of claim 97, wherein said cell is a dendritic cell.

25 99. The method of claim 98, wherein said dendritic cell is a Langerhans cell or cell line.

100. The method of claim 99, wherein said dendritic cell line is XS52 or XS106.

30 101. The method of claim 97, wherein said NTPDase is an ATPase and/or ADPase, an UTPase and/or UDPase, a CTPase and/or CDPase, a TTPase and/or TDPase, or a GTPase and/or GDPase.

102. The method of claim 97, wherein said cell expresses an ATPase.

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- 5 103. The method of claim 97, wherein said cell expresses an ADPase.
104. The method of claim 97, wherein said cell expresses an UTPase.
105. The method of claim 97, wherein said cell expresses an UDPase.
- 10 106. The method of claim 97, wherein said cell comprises an expression construct comprising a DNA segment encoding said NTPDase under the control of a promoter active in said cell.
- 15 107. The method of claim 97, wherein determining comprises measuring NTPDase activity of said cell.
108. The method of claim 107, wherein measuring NTPDase activity comprises:
 - a) culturing said cell in a culture solution comprising a nucleotide;
 - 20 b) determining the effect of said candidate substance on nucleotide levels in said culture solution; and
 - c) measuring a change in the nucleotide levels in said culture solution as compared to nucleotide levels in the absence of said candidate substance.
- 25 109. The method of claim 108, wherein said nucleotide is ATP and/or ADP and/or AMP, UTP and/or UDP and/or UMP, CTP and/or CDP and/or CMP, TTP and/or TDP and/or TMP, or GTP and/or GDP and/or GMP.
- 30 110. The method of claim 108, wherein said nucleotide is ATP and/or ADP and/or AMP.
111. The method of claim 108, wherein said nucleotide is UTP and/or UDP and/or UMP.

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- 5 112. The method of claim 108, wherein AMP levels are detected by chromatographic methods.
113. The method of claim 97, wherein measuring comprises measuring the NTPDase levels on the surface of said cell.
- 10 114. The method of claim 113, comprising an enzyme linked immunoassay using an enzyme-labeled anti-NTPDase antibody.
115. The method of claim 114, wherein the anti-NTPDase antibody is an anti-ATPase and/or anti-ADPase antibody, an anti-UTPase and/or anti-UDPase antibody, a anti-CTPase and/or anti-CDPase antibody, a anti-TTPase and/or anti-TDPase antibody, or a anti-GTPase and/or anti-GDPase antibody.
- 15 116. The method of claim 113, comprising fluorescent activated cell sorting of cells using a fluorescent-labeled anti-NTPDase antibody.
- 20 117. The method of claim 97, wherein determining comprises measuring a NTPDase mRNA level in said cell.
- 25 118. The method of claim 117, wherein measuring comprises Northern blotting.
119. The method of claim 117, wherein measuring comprises quantitative RT-PCR.
120. A method of screening for modulators of NTPDase-mediated immune responses comprising:
- 30 a) providing a cell that comprises an expression construct comprising a DNA segment encoding a screenable marker under the control of a promoter for a NTPDase;
- b) contacting said cell with a candidate substance; and

5 c) determining the effect of said candidate substance on expression of said selectable marker,

wherein a change in the expression of said selectable marker, as compared to selectable marker expression in the absence of said candidate substance, indicates that said candidate substance is a modulator of NTPDase promoter expression, and therefore a
10 modulator of NTPDase-mediated immune responses.

121. The method of claim 120, wherein said NTPDase-mediated immune responses is an immune response mediated by an NTPDase selected from the group consisting of CD39, CD39L1, CD39L2, CD39L3, CD39L4, Golgi-associated ecto-ATPase and ecto-
15 uridine diphosphatase (UDPase), lysosomal ecto-apyrase LALP70, hepatic canalicular ecto-apyrase, α -sarcoglycan and potato apyrase.

122. The method of claim 120, wherein said screenable marker is an enzyme and determining comprises measuring enzyme activity.

20 123. A method for treating a hyperactive immune response in a subject comprising administering to said subject a composition comprising a P2-receptor inhibitor.

124. The method of claim 123, wherein said P2-receptor inhibitor is an P2-receptor antagonist, an anti-P2-receptor antibody, an antisense P2-receptor oligonucleotide, or a
25 chemical substance.

125. The method of claim 123, wherein said P2-receptor inhibitor is an inhibitor of the P2X₁, P2X₄, P2X₅, P2X₇, P2X₁, P2Y₁, P2Y₁, P2Y₂, P2Y₄, P2Y₅, P2Y₆, P2Y₁₀, or P2Y₁₁
30 receptor.

126. The method of claim 123, wherein the P2-receptor inhibitor is an P2-receptor antagonist.

5 127. The method of claim 126, wherein the P2-receptor antagonist is suramin, KN-62, MRS2179, TNP-ATP, TNP-GTP, oxidized ATP, PPADS, Reactive Blue2.

128. The method of claim 123, wherein the antisense oligonucleotide comprises a nucleic acid that is complementary to a nucleic acid sequence encoding a P2X₁, P2X₄,
10 P2X₅, P2X₇, P2X₁, P2Y₁, P2Y₁, P2Y₂, P2Y₄, P2Y₅, P2Y₆, P2Y₁₀, or P2Y₁₁ receptor, or a fragment thereof.

129. The method of claim 123, wherein said hyperactive immune response is an allergic reaction.

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130. The method of claim 129, wherein said allergic reaction is allergic contact dermatitis, atopic dermatitis, allergic rhinitis (hay fever), bronchial asthma.

131. The method of claim 123, wherein said hyperactive immune response is an
20 autoimmune disease.

132. The method of claim 131, wherein said autoimmune disease is Addison's disease, alopecia, ankylosing spondylitis, antiphospholipid syndrome, Behcet's disease, chronic fatigue syndrome, Crohn's disease, ulcerative colitis, diabetes, fibromyalgia, Goodpasture
25 syndrome, Graves' disease, idiopathic thrombocytopenic purpura, lupus, Meniere's multiple sclerosis, myasthenia gravis, pemphigus vulgaris, primary biliary cirrhosis, psoriasis, rheumatoid arthritis, rheumatic fever, sarcoidosis, scleroderma, vasculitis, vitiligo, or Wegener's granulomatosis.

30 133. The method of claim 123, wherein said P2-receptor inhibitor is administered by topical, oral, intranasal, intratracheal, intraesophageal, intrabronchial, intra-vaginal, rectal intravenous, intraarterial, subcutaneous, or intramuscular routes.

134. A method for preventing a hyperactive immune response in a subject comprising
35 administering to said subject a composition comprising a P2-receptor inhibitor.

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135. A method for treating or preventing a hyperactive immune response in a subject comprising administering to said subject an expression construct comprising a DNA segment encoding a P2-receptor inhibitor under the control of a promoter active in cells of said subject.

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136. The method of claim 135, wherein said P2-receptor inhibitor is an inhibitor of the P2X₁, P2X₄, P2X₅, P2X₇, P2X₁, P2Y₁, P2Y₁, P2Y₂, P2Y₄, P2Y₅, P2Y₆, P2Y₁₀, or P2Y₁₁ receptor.

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137. The method of claim 135, wherein the P2-receptor inhibitor is an antisense molecule.

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138. The method of claim 137, wherein the antisense oligonucleotide comprises a nucleic acid that is complementary to a nucleic acid sequence encoding a P2X₁, P2X₄, P2X₅, P2X₇, P2X₁, P2Y₁, P2Y₁, P2Y₂, P2Y₄, P2Y₅, P2Y₆, P2Y₁₀, or P2Y₁₁ receptor, or a fragment thereof.

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139. The method of claim 135, wherein said expression construct is a viral expression construct.

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140. The method of claim 139, wherein said viral expression construct is selected from the group consisting of a retrovirus, an adenovirus, an adeno-associated virus, a herpesvirus, a polyoma virus, and a vaccinia virus.

141. The method of claim 135, wherein said expression construct is a non-viral expression construct.

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142. The method of claim 141, wherein said non-viral expression construct is administered as a naked DNA.

- 5 143. The method of claim 141, wherein said non-viral expression construct is administered in a liposomal formulation.